Coll. Antropol. **35** (2011) 3: 861–865
Original scientific paper

Croatia: Still a Low-Level HIV Epidemic? – Seroprevalence Study

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A B S T R A C T

Central Europe is a region with a low prevalence of infection with human immunodeficiency virus (HIV). Until the end of 2007, 663 HIV cases were recorded in Croatia, almost exclusively among most at-risk populations.The aim of this research was to determine the HIV prevalence among most at-risk populations and the level of the HIV epidemic in Croatia. According to the World Health Organization classification there are three levels of HIV epidemics: generalized (prevalence in general population >1%), concentrated (prevalence in general population <1% and prevalence in at least one of the most at-risk populations >5%) and low-level epidemic (prevalence in general population <1% and prevalence in each most at-risk population <5%). This was a research with convenience samples of most at-risk populations. The respondents were recruited by their peers, all non-governmental organizations that provide services for most at-risk populations and the researchers. Sera were tested using the fourth generation enzyme-linked fluorescent assay (EIA test) and reactive test were confirmed using the Western Blot test. In this research, the highest HIV prevalence was found within the men who have sex with men group (7/232=3%, 95%CI=1.3–6.3%) and commercial sex workers (1/70=1.4%, 95%CI= 1–7.8%). In these samples we were unable to determine whether Croatia is facing a low-level epidemic due to the fact that the prevalences were not statistically significantly lower than 5% (p=0.115 and p=0.1, respectively). For the remaining samples the prevalence was statistically significantly lower than 5%, which points to a low-level epidemic. The prevalences in these samples were 7/593=1.2% (95% CI=0.5–2.4%) in people with more than two sexual partners within the last 12 months, 2/249=0.8% (95%CI=0–2.9%) in people with sexually transmitted infections in history, 2/317=0.6% (95%CI=0–2.2%) in clients of sexual workers, 2/323=0.6% (95%CI=0–2.2%) in injecting drug users and 0.2% (95%CI= 0–1%) in the sample of migrant workers. Based on the results of this survey, Croatia would be classified as having a low-level HIV epidemic although the confidence limits in two most-at-risk groups, men who have sex with men and commercial sex workers, overlap 5%.

Key words: *HIV, risk, behavior, Croatia, Europe, prevalence*

Introduction

With the first cases of acquired immunodeficiency syndrome (AIDS) stigma has strongly and inseparably become attached to people infected with human immunodeficiency virus (HIV)[1] and has further spread onto many phenomena related to this infection: individuals, groups at higher risk for this infection, condom use, testing procedure but also onto general interest for HIV[2]. The importance of the stigma connected to HIV and risk behaviors is in fact that it strongly contributes to the problem of getting representative samples from most at-risk populations.

Unlike Eastern Europe, Central Europe still records either a low-level epidemic, or a concentrated epidemic[3]. Despite the low prevalence[4], wars and political instability with a consequential economic depression created surroundings in which changes in health behavior and lifestyles have occurred, mainly with respect to the increase in drug use and trade in sexual services, and with respect to more common migration of the population – all of which are prerequisites for accelerating the spread of the HIV infection[5]. Dominant transmission routes in this region are sexual relationships between men[3].

Received for publication February 10, 2009

The first HIV cases in Croatia were recorded in 1985, whereas towards the end of 2007 a total of 663 cases in which HIV was diagnosed HIV infection were recorded. In the same period, 270 of the infected have developed AIDS, out of which 141 died[6–8]. From the total number of HIV infected people, 80% are men, of which 65% were aged 25–44 at the time they were diagnosed. When routes of transmission are considered, 40% of the infections occurred through the male homosexual route, whereas almost equally many occurred through the heterosexual route of transmission. A little less than 10% of the infected acquire the infection through sharing equipment for injecting drug use and all the others routes of transmission (transfusion of infected blood, mother to child transmission) make up for less than 5% of the infected. Within the last several years, the homosexual route of transmission has been autochthonous while a considerable share of infections occurring through the heterosexual route of transmission is still related to infections acquired abroad[7].

The experience obtained during the first decade of combating HIV worldwide suggested the importance of work with the most at-risk populations both in countries with low and concentrated level of epidemics. In the whole world these populations include men who have sex with men (MSM), commercial sex workers (CSW), injecting drug users (IDU) and people deprived of their freedom[9]. A large majority of countries have also identified other populations at heightened risk, and for Croatia these additional groups are people with a history of sexually transmitted infections (HSTI) and seamen, i.e. migrant workers (MW), who have a crucial role in the heterosexual dissemination of non-B HIV 1 subtypes in Croatia[10,11].

Croatia is a country with low incidence and prevalence of HIV infection, and thus far no research in all most at-risk populations has been conducted. Hence, it is not known whether the HIV epidemic in Croatia is at a low-level or is it already concentrated. Only available data regarding HIV prevalence in most at-risk populations in Croatia are prevalence of 4.5% for the MSM population from Zagreb in 2006[12].

This research tried to give its contribution to an answer to this question and test the hypothesis that the HIV prevalence among each most at-risk population in Croatia is still lower than 5%.

Methods

This research was conducted as part of the project of the Ministry of Health and Social Welfare »Scaling-up response to HIV/AIDS in Croatia« in the period from December 1, 2003 until November 30, 2006. The project was financed through a donation of The Global Fund to fight AIDS, tuberculosis and malaria (GFTAM), so that the number of respondents was not limited and no financial interests were present that could influence the objectivity of the research.

According to the Croatian HIV surveillance data[7], the following populations were defined in this research as populations with the highest risk of acquiring HIV infection: MSM, CSW (both male and female), clients of commercial sex workers (CCSW), IDU, MW (Croatian seamen), HSTI (sexually transmitted infections for this research referred to viral hepatitis B and C, syphilis, gonorrhea, genital and anal herpes), people who had more than 2 sexual partners in the last 12 months (M2SP). Other known most at-risk population, such as refugees and uninformed personnel, were not found to be at high risk for HIV in Croatia.

All the respondents who were of age and willing to take part were recruited into the research (snow-ball, convenience sampling)[13]. The respondents were recruited by their peers, all non-governmental organizations that provide services for most at-risk populations and the researchers. We used all available channels to invite potential respondents into research. Only migrant workers, who were actually no hard-to-reach, were enrolled during regular health examination (consecutive sampling). The respondents were recruited on locations chosen on the basis of the results of a pilot study conducted in cooperation with the civil sector which provided us with a conclusion that a sufficient number of respondents could be recruited in Rijeka, Split, Zagreb, Zadar, Dubrovnik, Slavonski Brod and Osijek which enabled good geographical coverage across the whole country. Those cities are also the socializing centers of hard-to-reach populations from gravitating rural areas. Due to the size of the samples, data from different geographical locations were aggregated in the analysis. Researchers were epidemiology specialists in County Public Health Institutes and the Croatian National Institute of Public Health. The samples were collected continuously over a three years time period (Dec 2003–Dec 2006).

The respondents were included in pre- and post-testing counseling on HIV, gave informed consent, filled in an anonymous questionnaire and gave a sample of blood for HIV testing purposes. The questionnaire was designed to collect only basic socio-demographic data (gender, age) and information about most at risk-population respondents pertain to. The participants could choose one or more most at-risk groups to be classified in. For the purpose of prevalence calculation, participants were included in all groups they were self-classified. For example, if one stated to be MSM and M2SP he was included in both prevalences for MSM and M2SP, respectively. Researchers did not choose »main« most at-risk classification and they accepted straightforward self classification from the respondents.

In case of a positive test result, the respondents were referred to treatment with psychosocial support also available. This was a linked-anonymous research. The anonymity of the respondents was secured through coding of both the questionnaire and the serum: for each respondent a random number was generated, which was printed out in five copies on self-adhesive stickers. One copy was given to the respondent and represented a link

to his/her serum i.e. the testing result, the second copy was placed on the questionnaire, the third on the envelope in which the questionnaire was archived and the fourth and fifth copy were put on the vials into which blood was drawn, i.e. into which the serum was separated. Sera obtained through a centrifuge of full blood were transported following the cold chain protocol to the laboratory of the Croatian national Institute of Public Health where testing using the fourth generation enzyme-linked fluorescent assay (EIA test, HIV Duo Quick; BioMerieux, Marcy l,Etoile, France)[14] was conducted and in case of a positive screening test result a confirmatory test was conducted using the Western Blot test in the »Fran Mihaljević« Clinic for Infectious Diseases.

The planned sample size was 1200, i.e. about 200 for each most at-risk population. The sample size *per* population was calculated based on presumptions of the Z--test. We estimated that HIV prevalence in each sample would be less than 2% and calculated sample size which enables us to achieve statistical significance for the hypothesis that prevalence is lower than 5%.

The hypothesis that the HIV prevalence among each most at-risk population in Croatia is still lower than 5% was tested conducting the one-way Z-test[15]. The entering and analysis of data were conducted using the SPSS software package ver. 15.01 (SPSS ID: 729038).

Results

A total of 1361 respondents were included into the research, out of which 134 (9.8%) were female, 1215 (89.3%) male and for 12 (0.9%) respondents there was missing data on gender. The median year of birth was 1975 (31 years of age), interquartile range 17 years, the minimum being 1930 and maximum 1988 (Table 1).

The HIV prevalence among MSM and CSW was not significantly lower than 5% ($p=0.115$ and 0.1, respectively), while for the samples of IDU ($p<0.001$), MW ($p<0.001$), CCSW ($p<0.001$), M2SP ($p<0.001$) and HSTI ($p=0.002$) the prevalence was significantly lower than 5% (Table 2).

The percentage of overlapping among most-at risk populations higher than 10% of the sample was found for the following samples: MW and CCSW (13.08%), MSM and M2SP (13.01%), CCSW and M2SP (11.32%) and for IDU and M2SP (10.65%, Table 3).

Discussion and Conclusion

With a sample of 1361 respondent this research is the largest and most encompassing among all the research thus far conducted in Croatia in these populations. The gender and age distribution of the sample (men 89.3% and women 9.8% with the median age 31 and interquartile range of 18 years of age) approximately follow the same distribution of the HIV infected population in Croatia[7].

The prevalence of HIV among the MSM sample was 7/232=3% (95% CI=1.3–6.3%) and based on this sample, one cannot conclude that the prevalence is statistically significantly lower than 5%, i.e. on account of this population, Croatia might be facing a concentrated HIV epidemic. Since this was a convenience sample, one can assume that only those MSM decided to take part in the research who found themselves to have been at risk for an HIV infection, while for those who estimated to have been at little or no risk for an HIV infection we can assume to have withheld from taking part in the research. The other reason for possible higher prevalence in our sample than in the whole MSM population could be reaching urban population more than rural. If we assume that the size of the MSM population takes on several tens of thousands of people, it is not very likely that overall prevalence is around 3%.

The prevalence of positive anti-HIV tests in the IDU sample was 2/323=0.6% (95% CI=0–2.2%), which is statistically significantly lower than 5% and speaks for the conclusion that Croatia is facing no concentrated epidemics, particularly if we consider the fact that the above presented data are in accordance with data obtained through routine prevalence monitoring in this population.

The prevalence of HIV among MW was 1/537=0.2% (95% CI=0–1%), which is statistically significantly lower

TABLE 1
AGE AND GENDER DISTRIBUTION OF RESPONDENTS

Group	Gender[a] (Male/Female)	Age (median; interquartile range)
Men who have sex with men (MSM)	232/0	29; 9
Injecting drug users (IDU)	283/37	27; 8
Migrant workers (MW)	527/10	35; 17
Commercial sex workers (CSW)	55/14	31; 17
Clients of commercial sex workers (CCSW)	306/11	33; 18
Persons with more than 2 partners in the last 12 months (M2SP)	518/75	29; 10
Person with a history of sexually transmitted infection (HSTI)	194/53	35; 17
Total	1215/134	31; 17

[a]there was missing data on gender for 12 respondents, they were excluded from the table

TABLE 2
SEROPREVALENCE OF HIV AMONG MOST AT-RISK POPULATIONS AND THE RESULTS FOR TESTING HYPOTHESIS: THE PREVALENCE IN A GIVEN SAMPLE IS LESS THAN 5%

Group	Prevalence (%)	Confidence interval for prevalence (%)[a]	One-way Z-test[a]	p value for the Z-test
Men who have sex with men (MSM)	7/232 (3%)	1.3–6.3	1.2	0.115
Injecting drug users (IDU)	2/323 (0.6%)	0[b]–2.2	3.5	<0.001
Migrant workers (MW)	1/537 (0.2%)	0[b]–1	5	<0.001
Commercial sex workers (CSW)	1/70 (1.4%)	1–7.8	1.3	0.1
Clients of commercial sex workers (CCSW)	2/317 (0.6%)	0[b]–2.2	3.4	<0.001
Persons with more than 2 partners in the last 12 months (M2SP)	7/593 (1.2%)	0.5–2.4	4.2	<0.001
Person with a history of sexually transmitted infection (HSTI)	2/249 (0.8%)	0[b]–2.9	2.9	0.002

[a]$\alpha = 0.05$, [b]infinitely close to zero

TABLE 3
PERCENTAGE OF THE OVERLAPPING AMONG THE SAMPLES OF MOST AT-RISK POPULATIONS

	IDU[a]	MW[b]	CSW[c]	CCSW[d]	M2SP[e]	HSTI[f]
MSM[g]	1.84	0.88	0.81	1.76	13.01	1.54
IDU[a]		0.37	0.96	3.82	10.65	7.35
MW[b]			1.91	13.08	8.45	1.47
CSW[c]				3.67	2.87	1.10
CCSW[d]					11.32	3.89
M2SP[e]						7.13

[a]Injecting drug users, [b]Migrant workers, [c]Commercial sex workers, [d]Clients of commercial sex workers, [e]Persons with more than 2 partners in the last 12 months, [f]Person with a history of sexually transmitted infection, [g]Men who have sex with men

than 5% and speaks against the hypothesis of a concentrated epidemic in Croatia. This sample is the most representative of all the populations included in the research due to the fact that the respondents were recruited through regular health examinations in occupational medicine clinics.

The prevalence of HIV was 1/70=1.4% (95% CI= 1–7.8%) in the sample of CSW and 2/317=0.6% (95% CI=0–2.2%) with the sample of CCSW. For the sample of CCSW the prevalence was found to be statistically lower than 5%, while this could not be determined for the CSW. The sample of CSW proved to be the most hard to reach, and most of the sample is comprised of male respondents so the results must be taken with a pinch of salt. Having in mind the insufficient size of the sample and the fact that the samples of CSW and CCSW are hard to reach, it is by all means necessary to, along with quantitative research on a larger sample, implement the alternative – mostly qualitative – research methodology in these populations in Croatia.

The prevalence of HIV in HSTI respondents was found to be 2/249=0.8% (95% CI=0–2.9%) and in M2SP sample 7/593=1.2% (95% CI=0.5%–2.4%), both statistically significantly lower than 5%, which speaks against a concentrated epidemic. The main limitation of the results for the HSTI sample is a high degree of overlapping with the IDU sample (Table 3).

This research has provided us with the very first information on the most at-risk populations (except for MSM population) and consequently with a starting point for future research, it has also pointed out to the need for additional research in the CSW and MSM populations so that the level of HIV epidemics in Croatia may be determined.

The main limitation of this study is the generalizibility of the data, since this was a research with convenience sample. We cannot define the populations we had reached the samples from, so the results are rather informative than representative for most-at-risk populations in Croatia. But still, this research provides the information on over 1300 persons from most at-risk populations. The next limitation is the small sample of the respondents from the CSW population which makes the interpretation of the results for that sample very limited. Finally, there is an overlap between some samples and we cannot distinct which is the most important risk for those respondents. For example, for the respondent who is MSM and IDU and HIV infected we could not identify the route of infection between two risks.

In conclusion, this research would classify Croatia as a low-level HIV epidemic country although the confidence limits in two most-at-risk groups, men who have sex with men and commercial sex workers, overlap 5%. This is why it is necessary to conduct more comprehensive seroprevalence research in these populations, espe-

cially due to the results of the other research on MSM population from Zagreb[12]. Within samples of IDU, MW, CCSW, M2SP, and HSTI the seroprevalence of HIV was statistically significantly lower than 5%, which speaks against the hypothesis of a concentrated and is in line with the HIV epidemics in neighboring countries[3–5,16]. A qualitative and quantitative monitoring of risk behavior trends and seroprevalence of HIV in populations at highest risk from HIV infection seems to be a priority issue in prevention of HIV infection in Croatia.

Acknowledgements

The author would like to thank to Ira Gjenero-Margan for supervising the research, to all county epidemiologists for their invaluable help in data and samples collection, to Jasmina Pavlic for translating text to English and Kursat Levent Egriboz and Robert Conaty for English-language proof reading.

Source of funding for this research was a donation of The Global Fund to fight AIDS, tuberculosis and malaria to Croatia.

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HRVATSKA: DRŽAVA S NISKOM RAZINOM HIV EPIDEMIJE? – ISTRAŽIVANJE SEROPREVALENCIJE

SAŽETAK

Središnja Europa još uvijek bilježi epidemiju HIV-a niske razine. Do kraja 2007. godine, u Hrvatskoj je zabilježeno 663 slučaja infekcije HIV-om, gotovo isključivo u populacija s visoko rizičnim ponašanjima. Cilj ovog istraživanja bio je utvrditi prevalenciju HIV infekcije u populacijama s rizičnim ponašanjima i razinu epidemije u Hrvatskoj. Prema klasifikaciji Svjetske zdravstvene organizacije postoje tri razine HIV epidemije: generalizirana (prevalencija u općoj populaciji >1%), koncentrirana (prevalencija u općoj populaciji <1% i prevalencija u barem jednoj populaciji s povećanim rizikom >5%), te epidemija niske razine (prevalencija u općoj populaciji <1% i prevalencija u svakoj populaciji s povećanim rizikom <5%). Ovo istraživanje rađeno je na prikladnom uzorku populacija s najvećim rizikom. Ispitanici su regrutirani putem istraživača, kao i svih nevladinih organizacija koje pružaju usluge populacijama s najvećim rizikom. Serumi su testirani četvrtom generacijom fluorescentnog enzim-vežućeg eseja (EIA test), a reaktivni nalazi potvrđeni su Western blot testom. Najviša prevalencija pronađena je u populaciji muškaraca koji prakticiraju seks s muškarcima (7/232=3%, 95%CI=1,3–6,3%), i populaciji prodavatelja/ica seksualnih usluga (1/70=1,4%, 95%CI=1–7,8%). Za ta dva uzorka nismo uspjeli dokazati epidemiju niske razine, odnosno prevalencija nije bila statistički značajno niža od 5% (p=0,115 i p=0,1). Za ostale uzorke populacije s rizičnim ponašanjima prevalencije su bile statistički značajno niže od 5% što ukazuje na epidemiju niske razine. Utvrđene su slijedeće prevalencije HIV infekcije: 7/593=1,2% (95% CI= 0,5–2,4%) u ispitanika s više od dva seksualna partnera/ice u zadnjih godinu dana, 2/249=0,8% (95%CI=0–2,9%) u ispitanika s drugom spolno prenosivom bolešću u anamnezi, 2/317=0,6% (95%CI=0–2,2%) u klijenata/ica prodavatelja/ica seksualnih usluga, 2/323=0,6% (95%CI=0–2,2%) u osoba koje injiciraju droge i 0,2% (95%CI=0–1%) u populaciji radnika/ica migranata. Prema rezultatima ovog istraživanja Hrvatska je i dalje zemlja s niskom razinom HIV epidemije, iako gornje granice intervala pouzdanosti u dva uzorka (muškarci koji prakticiraju seks s muškarcima i prodavateljice seksualnih usluga) prelaze 5%.